New Strategies for Bladder and Prostate Cancer, BPH Explored by South Central Urologists

Highlights from the South Central Section of the American Urological Association
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The 1998 meeting of the South Central Section of the American Urological Association actually took place in 1999. The meeting, originally scheduled for Cancun on the Yucatan Peninsula, Mexico, was canceled because of Hurricane Mitch. It was then rescheduled for January at the same location in a different venue. Unfortunately, several abstracts had to be withdrawn because the speakers could not attend the rescheduled meeting. Despite this, Cancun proved to be a beautiful location.

The main topics of the meeting were diagnosis and treatment of bladder and prostate cancer, benign prostatic hyperplasia, urinary dysfunction, and continence and endourologic issues.

Benign Prostatic Hyperplasia (BPH)

The transurethral needle ablation (TUNA) procedure for patients with lower urinary tract symptoms (LUTS) and clinical BPH was featured in 2 presentations,[1,2] both analyzing the data of the US Multi-Center, Randomized Study in which TUNA is compared with a standard transurethral radical prostatectomy (TURP). In this trial, conducted in 5 academic medical centers in the United States, 65 patients were treated with the TUNA device, and 56 patients received a TURP.[1] To make the data as comparable as possible, the TUNA procedure was performed according to a strict protocol regarding the number of lesions, depending on the length of the prostatic urethra. The TURP was performed by the principal investigator at each institution or by a chief resident under direct supervision. Although not all patients were available for a 2-year follow-up, 68% of the TUNA-treated patients had complete follow-up data for 24 months, as did 55.4% of the TURP-treated patients. More than 30% improvement in the American Urological Association (AUA) symptom score was experienced by 62% of the TUNA patients, compared with 77% of the TURP patients. Similarly, a >30% improvement in the quality-of-life score (0 to 6 scale) was realized by 70% of the TUNA patients versus 80% of the TURP patients. While the data regarding symptoms, bother, and quality of life were comparable between the 2 treatment groups, the improvement in peak urinary flow rate was significantly better in the TURP group. However, as a tradeoff, significantly fewer adverse events were noted in the TUNA-treated patients, and none occurred after 6 months of follow-up. Adverse events in the TUNA-treated patients were, in general, mild and transient in nature.

In the companion presentation, Fritzsch and colleagues analyzed the effect of TUNA and TURP on pressure-flow urodynamic parameters.[2] The conduct of pressure-flow urodynamic studies in multicenter, randomized trials is always very difficult. First, one has to assure that the pressure-flow data from all centers are comparable. A total of 121 patients were available for analysis. The key parameter of interest was the detrusor pressure at the moment of peak urinary flow rate as well as the Abrams-Griffith number (mathematically derived by subtracting the peak urinary flow rate multiplied by 2 from the detrusor pressure at the moment of the maximum flow rate). At baseline, there were no significant differences between the TUNA and TURP patients, or between the patients treated at the various academic centers. Thus, it appeared to be permissible to pool the data for combined analysis.

At baseline, the peak detrusor pressure at the moment of maximum flow rate was 78.7 and 75.8 cm H_20 for the TUNA and TURP groups, respectively (nonsignificant difference). The Abrams-Griffith number was 52.5 and 52.7 for the 2 groups (not significant). At 6 months of follow-up, the P_{det} at Q_{max} had decreased to 64.9 and 53.7 for the TUNA- and the TURP-treated patients (both differ-

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ences from baseline significant); the Abrams-Griffith number had decreased to 21.4 and -8.2 for the TUNA and TURP groups (both differences from baseline significant, between groups significant at $P<.001$). Free, maximum urinary flow rate improved from 8.9 to 13.5 mL/s in the TUNA-treated patients, and from 8.8 to 20.6 mL/s in the TURP-treated patients (both differences from baseline significant, difference between groups significant at $P<.001$).

The conclusion from these 2 presentations is that the TUNA procedure appears to be effective and durable at 2 months, at which time approximately two-thirds of all patients are available for follow-up. Urodynamic parameters change significantly less than those following TURP. The issue—whether changes in peak urinary flow rate are relevant to patients—remains unresolved, as does the issue of whether changes in invasive urodynamic parameters have negative predictive value toward future outcomes.

Gurevitch and colleagues looked at improving patient flow in a busy BPH or clinical research clinic.[3] Many investigators working in the field recognize that often patients' duration of stay in the clinic is delayed by their inability to provide an adequate voided volume for the flow rate recording. In most clinical trials, a voided volume of >125 mL or even 150 mL is mandated for the flow rate to be valid. In this study, 99 volunteers with a mean age of 54 years (range, 38-80 years) were enrolled in a randomized, open-label study in which they were asked to perform 2 flow rate recordings on 2 different days with a crossover. The patients were randomized to either receive no premedication or 20 mg of furosemide on arrival at the clinic. Those patients receiving furosemide on their first visit received no premedication on their second visit, and vice versa.

There was an increase in the voided volume from the first to the second flow rate recording (277 vs 311 mL, $P=.04$), and an increase in the maximum urinary flow rate (19.8 vs 21.2, $P=.02$). This is attributable to some learning effect—that the patients, independent of taking a diuretic prior to performing the flow rate recording, improved their "performance" during their second visit. However, between the first and second visit independent of randomization to a diuretic, there was no difference in the wait time prior to performing the flow rate (111 vs 120 minutes, $P=.9$). Quite in contrast, however, when the patients were stratified by a nondiuretic versus a diuretic flow rate independent of the sequence in which these tests were done, a significant increase in voided volume was noted (269 vs 318, $P<.01$), with no significant difference in peak urinary flow rate (19.9 vs 21.1 mL/s, $P=.058$). The most significant finding of this study was the significant reduction in the wait time from 155 to 80 minutes ($P<.001$). Thus, it appears that by giving patients a diuretic on arrival at the clinic, the wait time can be reduced by 50%, while not affecting the validity of the flow rate recording. Parenthetically, most investigators, and certainly their research coordinators and research nurses, know which patients are unlikely to produce a required volume. Since, in most clinical research studies, flow rates are repeated at several visits, the research nurses become familiar with a patient's pattern, and it might prove quite helpful to administer a diuretic on arrival to those patients unlikely to perform at the required volume.

Two presentations dealt with medical therapy for LUTS and BPH. Roehrborn and associates presented data from the 4-year, placebo-controlled trial comparing finasteride with placebo (Proscar Long-Term Efficacy and Safety Study).[4] In this study, 3040 patients with enlarged prostates on digital rectal examination (DRE) and moderate to severe LUTS were enrolled in a 4-year, double-blind, placebo-controlled study conducted at numerous US centers. In this analysis, AUA symptom score data were presented stratified by baseline serum prostate-specific antigen (PSA) and baseline prostate volume. The patients were divided into tertiles based on PSA (0 to 1.3, 1.4 to 3.2, 3.3 to 12 ng/mL ; 14 to 41, 42 to 57, 58 to 222 mL, respectively). The main finding, corroborating the results of a meta-analysis of all 1-year data from 6 placebo-controlled finasteride trials, showed that the difference between finasteride and placebo is not evident in patients in the lower PSA and lower prostate volume strata. In fact, in the lowest PSA tertile—patients with a serum PSA level between 0 and 1.3 ng/mL—the mean difference in terms of symptom score improvement was -0.5 points (not significant). However, in the second and third PSA strata, the mean difference was -2.8 and 3.1 points, respectively ($P<.001$). While there is an increase in the efficacy of finasteride in men with larger prostates and higher serum PSA levels, the reduction in the placebo response is equally as much responsible for the increase in the difference between finasteride and placebo. This study and others for the first time highlight that the natural history of the disease is predicated on baseline volume and serum PSA: ie, patients with higher serum PSA levels and larger prostate volumes experience more deterioration of symptoms (as well as urinary flow rate) than those men with smaller prostates and lower PSAs.

A randomized, double-blind study by MacDiarmid and colleagues assessed the optimal dose of doxazosin in patients with LUTS and BPH.[5] This study addresses, in innovative fashion, the question of whether 4 or 8 mg is the optimal dosage. In this study, 112 patients with LUTS and

BPH who had clinically improved on 4 mg of doxazosin were randomized to either continue on 4 mg or to increase to 8 mg. At the time of the analysis, 82 patients had completed the study, and, of those, 42 patients continued on 4 mg, and 40 patients increased to 8 mg. Both groups were similar in respect to age, baseline AUA symptom score, and peak flow rate. The mean improvement from baseline in the AUA symptom score was 1.6±5.3 and 5.3±8.0 for the 4 and 8 mg groups (*P*=.03). Maximum flow rate improved by +0.6±6.4 and 1.4±7/9 in the 4 and 8 mg groups, respectively. Of the 4 and 8 mg groups, 36.1% versus 71.9% preferred the new dosage over the original 4 mg dosage. An equal number of patients dropped out because of adverse events or other reasons, and there was no statistical difference in side effects. This interesting study design lends credence to the notion that the higher doses of α-adrenergic receptors (8 mg of doxazosin and 10 mg of terazosin) are the preferred dosage for men with LUTS and BPH. Most certainly, every physician dealing with patients with BPH and utilizing α-adrenergic receptor blockers should increase the dose of terazosin and doxazosin to at least 8 and 10 mg if patients have insufficient improvement in symptoms prior to abandoning this form of therapy.

Ramsey and colleagues analyzed differences in response to microwave thermotherapy in men with BPH depending on whether they were previously treated with α-adrenergic receptor blockers.[6] The premise for this analysis is that the mechanism of action of microwave thermotherapy is not completely understood. It has been postulated that the heat preferentially destroys nerve tissue, and, specifically, α-receptors, thus, in essence, inducing a permanent state of α-blockade with resulting symptom improvement. There are data from various trials on 490 patients treated with the TARGIS system (Urologix) who had AUA symptom scores available at baseline and at 6 months. In this analysis, the data were pooled across trials and stratified by whether or not the patients had received prior α-blocker therapy. Altogether, there were 262 patients with no prior α-blocker therapy versus 88 patients who at some time had been treated with α-blocking agents for varying periods. Interestingly, at baseline the AUA symptom score was 20.7 and 22.0 for patients without versus with prior α-blocker therapy (*P*=.07). Peak urinary flow rate was nearly identical at 7.6 mL/s and 7.1 mL/s for both groups, respectively. However, at 6 months, the AUA symptom index was reduced to 7.6 and 12.2 points for the patients without and with prior α-blocker therapy, respectively (*P*<.001). While both groups experienced a significant decrease in symptom severity from baseline, the group without prior α-blocker therapy experienced a significantly greater decrease compared with those patients who, at some point, had been pretreated with α-adrenergic blockers. A possible confounding factor was that baseline serum PSA was significantly lower in those patients who had been treated previously with α-receptor blockers, although it is not known what impact this might have on the outcome of the microwave thermotherapy. While this cannot be the definite answer to the question, it is an intriguing finding. The difference in the magnitude of improvement may be due to patient selection, different responses in patients already dissatisfied with α-blocker therapy, or the composition of the prostate tissue (glandular versus stromal). However, it is also possible that in those patients in whom medical α-receptor blockade has already been effected, heat-induced α-receptor elimination is less effective. It is hoped that further research will focus on the exact mechanism of action of microwave thermotherapy to help us understand better how to utilize this treatment and define treatment outcomes predictors. Ultimately, identifying outcomes pre-

Key words

Transurethral needle ablation (TUNA) • Transurethral resection of the prostate (TURP) • Transrectal ultrasound (TRUS) •Prostate-specific antigen (PSA) • Benign prostatic hyperplasia (BPH) • Alpha blockade •

Main Points

- The TUNA procedure for patients with BPH appears effective and durable at 2 months.
- Patients with BPH who have higher serum PSA levels and larger prostate volumes have more symptom deterioration than those with smaller prostates and lower PSA levels over time.
- Nerve sparing in radical prostatectomy does not raise the risk of disease recurrence.
- Patients at high risk of prostate cancer are candidates for more aggressive biopsy strategies even after 2 negative standard sextant biopsies.
- Prostate cancer patients should be treated according to grade and stage, regardless of race.
- In patients receiving hormone manipulation prior to radiation therapy or brachytherapy for prostate cancer, PSA suppression seen 6 to 12 months after later may be due to the hormone manipulation, rather than the radiation therapy or brachytherapy.

dictors will help in reducing treatment failures and re-treatment rates, and will help improve cost-effectiveness of therapy.

Bladder Cancer

The question of tumor control in nerve-sparing radical cystoprostatectomies was raised from Naughton and associates at Washington University in St. Louis.[7] Thirty-three men with the mean age of 66 years (range, 45-75 years) with organ-confined bladder cancer underwent radical cystoprostatectomy by 1 surgeon (Dr. Andriole). In 20, a nerve-sparing technique was used, and in 13, a standard, non–nerve-sparing technique. The men who received the nerve-sparing technique were significantly younger (63 vs 71 years, *P*=.02), most likely due to selection bias. Pathologic evaluation of specimens revealed no statistical difference between the 2 groups regarding grade 3 or 4 tumors, advanced stage, or margin positivity. At a mean follow-up of 30 months, there was no difference in recurrence rate either. These data from a nonrandomized group of patients in the hands of 1 experienced surgeon would suggest that the nerve-sparing technique does not increase the risk of margin positivity or disease recurrence. Thus, younger men interested in preserving sexual function can be counseled appropriately that an attempt at nerve-sparing radical cystoprostatectomy does not compromise cancer surgery per se.

The issue of cystectomy in transitional cell carcinoma of the bladder has seemingly been put to rest. However, in other forms of bladder cancer, it remains an open issue, such as in patients with adenocarcinoma of urachal origin. Fagelson and Sagalowsky reviewed 11 patients who were treated at The University of Texas Southwestern Medical Center and affiliated hospitals.[8] There were 7 male and 4 female patients with the mean age of 44 years who presented with hematuria (82%) and irritative symptoms (64%). Of the patients who underwent partial cystectomy for organ-confined disease, 75% are currently with no evidence of disease at a mean follow-up of 58 months (range, 8-132 months). Both recurrences occurred in those patients in whom the bladder had been opened during surgery, as opposed to those patients in which the bladder was resected closed between 2 clamps. All patients who had non–organ-confined disease had recurrences, including 1 with nodal disease who underwent partial cystectomy without bladder opening. This patient had partial response with 3 courses of MVAC (methotrexate, vinblastine, doxorubicin, cisplatin) chemotherapy. The authors conclude that partial cystectomy with preservation of the organ offered a relatively high cure rate for patients with organ-confined disease. In fact, removing the tumor between 2 clamps without opening the bladder may decrease the risk of recurrences as long as there are negative margins. Those patients in whom the disease is outside the bladder have a dismal prognosis regardless of what procedure is chosen.

Prostate Cancer

The issue of prostate cancer diagnosis, refinements of transrectal ultrasound (TRUS)-guided biopsy techniques, and the issues of serum PSA and derivatives dominated the session on prostate cancer diagnosis. It is well known that of men who have a negative biopsy guided by TRUS and who have an elevated PSA, a significant number will have a positive biopsy if they undergo a second set of TRUS-guided biopsies. In fact, it is estimated that of all patients with a negative TRUS-guided biopsy, between 15% and 25% will have a positive biopsy on a second TRUS-guided biopsy.

Dundore and associates from Jacksonville suggested a novel biopsy technique to increase a sampling from anatomic regions not usually biopsied.[9] To this end, 20 patients at high risk for cancer (persistently elevated PSA or previously diagnosed high-grade prostatic intraepithelial neoplasia) who had 2 sets of negative sextant biopsies were extensively biopsied under general anesthesia by a transperineal template-guided technique. Using this technique, 35% of the patients were ultimately found to have prostatic adenocarcinoma. Those patients with a higher total serum PSA and/or a higher PSA density had even a higher rate of cancer detection. Of significance is the fact that, while 21 of a total 304 biopsies obtained in these patients contained cancer, 11 of them were in areas that are out of reach by standard biopsy technique. It is also noteworthy that 71% of the patients found with cancer had a Gleason grade of 7 or higher, thus representing a significant clinical cancer burden. These data suggest that patients—even after 2 negative standard sextant biopsies—who were considered at high risk and in whom the treating physician maintains a high index of suspicion might be suitable candidates for a considerably more aggressive biopsy strategy. How these data would compare with other strategies suggested in the literature, such as increasing the number of biopsies by standard TRUS-guided techniques, obtaining lateral biopsies, or transition zone biopsies, remains to be seen, since no direct comparison has been performed.

Many men will ask their physician how painful a TRUS-guided biopsy might be. My usual response would be that it is just a very short, sharp sensation that usually goes away rather quickly. However, having no personal experience with this, it was interesting to see actual data presented by the group from Washington University.[10] One hundred and thirty men with PSA levels between 5 and 20 were randomized prospectively to

undergo either 6 or 12 prostate biopsies under TRUS guidance, and they were evaluated with a self-administered pain questionnaire. The score ran from 0 to 10, 0 representing no discomfort, and 10 the most severe discomfort. Immediately following and 2 weeks after the biopsy, the patients were asked regarding the pain during probe insertion, needle insertion, rectal pain, abdominal pain, and overall pain. There were no significant differences in pain scores between the 6 and 12 core groups, either immediately or at 2 weeks of follow-up. Patients, in general, reported the pain as mild to moderate. The overall pain score immediately following the biopsy was on average 3.1 and 3.3 for the 6 and 12 core groups, respectively. There was no statistical difference in the incidence of hematuria, but there was a significant increase in hemospermia from 63% to 80%, and hematochezia from 6% to 20% in the 6 versus the 12 biopsy group, respectively. The cancer detection overall for both groups was 30%, and it was not significantly different between the 2 groups. Another interesting observation is that there was not much difference in pain perception between the insertion of the probe and the insertion of the needle, which is somewhat a surprise as one might have guessed that the actual needle insertion is the more painful act.

Data from a prospective, multicenter clinical trial evaluating the percent free PSA (%fPSA) and the differentiation of prostate cancer from benign disease were presented by Slawin and colleagues on behalf of the multicenter group representing several academic institutions across the country.[11] Thirty-two thousand men were screened and 773 subjects were enrolled at 7 medical centers. These subjects had a nonsuspicious rectal examination and a PSA level between 4 and 10. Sextant biopsies were performed in all patients. At a cut point of 25% fPSA, 95% of cancers were detected, and 20% of men without cancer would have been spared a biopsy. %fPSA increased as patient age increased, and an inverse relationship was found between %fPSA and total PSA (tPSA) that did not affect cut points within the range of 4 to 10 ng/mL. In this screening population, a single cut point of 25% worked well regardless of age, prostate size, or PSA level within the specified range between 4 and 10 ng/mL. %fPSA proved to be an independent predictor of prostate cancer and contributed significantly more than age or PSA level. For tPSA in the range of 4 to 10 ng/mL, the probability of cancer was 56% if the fPSA was 0% to 10%, 28% if %fPSA was 10% to 15%, 20% if it was 15% to 20%, 16% if it was 25%, and 8% only if it was >25%.

The issues of PSA, race, and prostate cancer detection were presented by Ford and associates from the University of Texas Southwestern Medical Center in Dallas.[12] Six hundred and ninety-four patients who underwent TRUS-guided biopsies to rule out prostate cancer at the Dallas VA Medical Center formed the basis for this report. Approximately one-fourth of the population were African American. The overall cancer detection rate was 39.3%. There was no difference regarding age (67 vs 66 years), prostate volume (39 mL vs 42 mL), between African American and Caucasian men. However, African American men had a higher tPSA (8.6 ng/mL vs 6.5 ng/mL, $P<.001$). The prostate cancer detection was 46.6% in African American men versus 36.8% in Caucasian men ($P=.028$ by chi square). Interestingly, both tPSA and PSA density performed better in African American patients than in Caucasian patients. The area under the curve for the receiver operating characteristic curves was 0.729 versus 0.838 (Caucasians vs African Americans) for a tPSA, and 0.800 and 0.874 for PSA density.

Following up on this theme, Witte and colleagues from the Scott Department of Urology in Houston presented data regarding margin positivity and its relationship to race.[13] One thousand, one hundred and forty-five patients had undergone radical prostatectomies, of which the majority (1104) were Caucasians. Clinical stage, Gleason grade, PSA level, race, and surgical margin status were available. After controlling for clinical stage, Gleason sum, and preoperative PSA, multiple logistical regression analyses demonstrated that race was not an independent predictor of positive surgical margins. Additionally, data have been presented to demonstrate there was no stage for stage difference in survival between African American and Caucasian patients; taken together with these data, the combined data suggest the local biologic behavior of prostate cancer is not influenced by race, and that differences in the natural history are likely due to a complex interaction of ethnic factors. The recommendation of the investigators is that patients with prostate cancer be treated according to their grade and stage in a similar fashion regardless of race.

Ziada and associates from the University of Colorado Health Sciences Center reported their experience utilizing a perineal approach to salvage prostatectomy following failed radiation therapy.[14] Twelve patients had failed radiation therapy, 11 of whom elected to undergo perineal salvage prostatectomy. Only 1 patient had a rectal injury (8.3%). The average blood loss was 533 mL, and no patient required a blood transfusion. Positive surgical margin was only found in 3 (25%) patients, and a failure as determined by a rise in PSA level occurred in 3 of 12 patients as well. Complete preservation of continence was achieved in 7 patients; 5 patients lost their potency and had

variable degrees of incontinence. One might expect that with the increasing use of external beam radiation and brachytherapy, a larger number of patients will seek help for a biochemical recurrence in the future. These patients present a formidable challenge for any physician. Choices range from conservative management, hormonal therapy, cryosurgery, other heat-induced forms of tissue ablation, but certainly should include the option of a salvage prostatectomy in men carefully chosen based on their age, their initial tumor stage and grade, and their comorbidities. In patients fully recognizing the potential problems associated with salvage prostatectomy, this approach might be a useful tool in our armamentarium. It is clear that for many patients who had undergone external beam radiation, had biochemical recurrence, and elected to proceed with a salvage prostatectomy using the retropubic route, a lymph node dissection is all but impossible. Thus, the 1 advantage of a retropubic approach over a perineal prostatectomy—namely the ability to perform a lymph node dissection—really is more or less irrelevant in this setting.

Mackenzie and associates reported on a novel form of treatment for biochemical failure following presumed curative treatment for localized disease.[15] Thirty-nine men ranging in age from 54 to 88 years underwent hormonal manipulation with finasteride 5 mg bid and flutamide 125 mg po bid for PSA failure following treatment of apparently clinically localized prostate cancer. The mean follow-up was 19.2 months, with a range from 4 to 35 months. At the beginning of hormonal manipulation, the mean PSA level was 6.75 ng/mL; a mean nadir PSA of 0.7 ng/mL was reached on average at 5.8 months. Twenty-five of the patients developed breast tenderness and/or breast enlargement, and 5 reported gastrointestinal disturbances. Nine patients who were potent prior to the start of hormonal manipulation remained potent throughout the treatment.

It is clear this form of hormonal manipulation cannot induce a cure for a desperate situation—namely, a failure to achieve clearance of the disease in a presumed localized disease state. We are all confronted with these patients in ever-increasing numbers. While some patients are content with watching their PSA level and not undertaking immediate aggressive therapy, others are quite desirous of a therapeutic intervention. This regimen, consisting of a dose of finasteride twice that recommended for BPH (5 mg bid) and flutamide at a reduced dose (125 mg bid), is apparently relatively well tolerated, perhaps, quite importantly, preserves potency, and achieves 1 important goal—namely, to reduce the PSA level. Whether this treatment provides long-term cancer control and improves both cause-specific and/or overall survival remains to be seen.

A provocative study was presented by Fritzsch and colleagues from the University of Texas Southwestern Medical Center in Dallas.[16] There were several settings in which it would be interesting to know the precise time line of the PSA response to hormonal manipulation and the cessation of such manipulation—ie, stopping luteinizing hormone-releasing hormone (LHRH) analogues or total androgen ablation. It is known from older literature that, in many patients who have taken diethylstilbestrol for many years, testosterone would never increase above castrate levels due to permanent damage of the testicular parenchyma. Similar studies have not been performed utilizing LHRH analogue treatment. However, clinical assumptions are being made in trials in which patients undergo intermittent hormonal manipulation and certainly in patients who undergo radiation therapy with neoadjuvant hormonal manipulation. In such trials, it is commonplace to pretreat patients with hormonal manipulation, then perform either radiation therapy or brachytherapy, discontinue hormonal manipulation, and monitor the PSA level and attempt to assess the efficacy of radiation therapy/brachytherapy based on the PSA changes. The question remains, however, whether the radiation therapy/brachytherapy can take full credit for the PSA changes seen at 6, 9, and 12 months or whether, perhaps, these changes are still induced by the hormonal therapy. To answer this question at least in a limited fashion, 14 patients enrolled in a pilot trial, all of whom had been on LHRH analogue therapy for at least 2 years (range, 25-82 months). All patients had, at study entry, castrate levels of testosterone with a median of 10 ng/dL and suppressed levels of LH. All patients signed informed consent documents and discontinued LHRH therapy. In monthly intervals, measurements of serum hormones (testosterone, LH, follicle stimulating hormone) and serum PSA were performed

The findings were that the testosterone levels did not increase significantly until 6 months of follow-up. There was also no significant change in PSA levels from baseline up to 6 months of follow-up. In fact, even out to 12 months, the predefined end point of the study at which every patient was placed back on hormonal withdrawal, several of the patients had testosterone levels remaining in castrate ranges. This study would suggest that at least in a subset of patients undergoing neoadjuvant hormonal therapy, the PSA suppression seen at 6 or 12 months of follow-up may not be due to the radiation therapy or brachytherapy, but rather due to a lasting effect of the hormonal manipulation. While of interest and provocative in themselves, these data certainly need further confirmation, perhaps in multicenter studies. □

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